

Atty. Docket No. 2001-1797A
Serial No. 10/000,096
May 18, 2005

AMENDMENTS TO THE CLAIMS:

Claim 1 (Currently Amended): An antibody that recognizes an active hepatocyte growth factor activator (HGFA) activated by limited proteolysis of inactive HGFA, which is a precursor of active HGFA, between arginine at a position of 407 and isoleucine at a position of 408 which correspond to amino acid positions 13 and 14 of SEQ ID NO: 3 as counted from a translation initiation amino acid of inactive HGFA, and has a dissociation constant of 1×10^{-5} M or higher for inactive HGFA and a dissociation constant of 1×10^{-8} M or lower for active HGFA.

Claim 2 (Previously Presented): The antibody according to Claim 1, which has a dissociation constant of 1×10^{-9} M or lower for active HGFA.

Claim 3 (Original): The antibody according to Claim 1 or 2, which is a monoclonal antibody.

Claim 4 (Previously Presented): The antibody according to Claim 3, which recognizes active HGFA having a molecular weight of about 34,000-98,000 determined by the SDS-PAGE method.

Claim 5 (Previously Presented) The antibody according to Claim 4, which recognizes active HGFA having a molecular weight of about 34,000-38,000 determined by the SDS-PAGE method.

Claim 6 (Original): The antibody according to Claim 4, which is produced by a hybridoma of an accession number FERM BP-7779.

Claim 7 (Previously Presented): A monoclonal antibody that recognizes active HGFA activated by limited proteolysis of inactive HGFA, which is a precursor of active HGFA,

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between arginine at a position of 407 and isoleucine at a position of 408 which correspond to amino acid positions 13 and 14 of SEQ ID NO: 3 as counted from a translation initiation amino acid of inactive HGFA, and has a dissociation constant of 1×10^{-5} M or higher for inactive HGFA and a dissociation constant of 1×10^{-8} M or lower for active HGFA.

Claim 8 (Previously Presented): The monoclonal antibody according to claim 7, which has a dissociation constant of 1×10^{-9} M or lower for active HGFA.

Claim 9 (Original): A hybridoma cell line that produces a monoclonal antibody according to Claim 3.

Claim 10 (Original): A hybridoma cell line that produces a monoclonal antibody according to Claim 7.

Claim 11 (Currently Amended): A hybridoma cell line that produces the **[[a]]** monoclonal antibody according to Claim 8.

Claims 12-22 (Cancelled).

Claim 23 (Currently Amended): A kit for detecting or measuring active HGFA, which comprises one or more antibodies that recognize an active ~~hepatocyte-growth-factor-activator (HGFA)~~ HGFA activated by limited proteolysis of inactive HGFA, which is a precursor of active HGFA, between arginine at a position of 407 and isoleucine at a position of 408 which correspond to amino acid positions 13 and 14 of SEQ ID NO: 3 as counted from a translation initiation amino acid of inactive HGFA, and has a dissociation of 1×10^{-5} M or higher for inactive HGFA and a dissociation constant of 1×10^{-8} M or lower for active HGFA.

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Claim 24 (Previously Presented): The kit according to Claim 23, wherein the one or more antibodies has a dissociation constant of 1×10^{-9} M or lower for active HGFA.

Claim 25 (Currently Amended): The kit according to Claim 23, wherein the kit further comprises an active HGFA activated by limited proteolysis of inactive HGFA, which is a precursor of active HGFA, between arginine at a position of 407 and isoleucine at a position of 408 which correspond to amino acid positions 13 and 14 of SEQ ID NO: 3 as counted from a translation initiation amino acid of inactive HGFA.

Claim 26 (Original): The kit according to any one of Claims 23 to 25, which is used for the diagnosis of disease selected from the group consisting of organ inflammation, glomerular nephritis, cancer, myocardial infarction, angina pectoris, cerebral infarction or thrombosis.

Claim 27 (Original): The kit according to any one of Claims 23 to 25, which is used to measure active HGFA in a biological component collected from a subject suspected of having a disease.

Claim 28 (Original): The kit according to any one of Claims 23 to 25, wherein the active HGFA is detected or measured by immunostaining.

Claims 29-32 (Cancelled).

Claim 33 (Currently Amended): A method for producing an antibody that recognizes an active HGFA and has a dissociation constant of 1×10^{-5} M or higher for an inactive HGFA and a dissociation constant of 1×10^{-8} M or lower for an active HGFA, comprising the steps of:

(i) immunizing a mouse with an active HGFA as an antigen to produce antibody-producing cells in the spleen or lymph node of said immunized mouse,

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- (ii) collecting antibody-producing cells from the spleen or lymph node of said immunized mouse;
- (iii) fusing the antibody-producing cells with rat myeloma cells to produce hybridomas,
- (iv) selecting hybridomas producing the antibody that recognizes an active HGFA activated by limited proteolysis of inactive HGFA, which is a precursor of active HGFA, between arginine at a position of 407 and isoleucine at a position of 408 which correspond to amino acid positions 13 and 14 of SEQ ID NO: 3 as counted from a translation initiation amino acid of inactive HGFA, and has a dissociation constant of 1×10^{-5} M or higher for an inactive HGFA and a dissociation constant of 1×10^{-8} M or lower for an active HGFA, and
- (v) culturing the selected hybridomas in a medium and collecting the antibody from the supernatant of the medium.